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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,187	09/25/2002	Caroline Dean	0380-P02825USO	8783

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EXAMINER	
BAUM, STUART F	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 09/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,187	DEAN ET AL.	
	Examiner	Art Unit	
	Stuart F. Baum	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-4 and 7-34* is/are pending in the application.

4a) Of the above claim(s) *4,7,9-15,25-29,33 and 34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-3, 8, 16-24, and 30-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 September 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed 6/30/2005 has been entered.

2. Claims 2-4 and 7-34 are pending.

Claims 1 and 5-6 have been canceled.

Claims 4, 7, 9-15, 25-29, and 33-34 have been withdrawn from consideration for being drawn to non-elected inventions.

3. Claims 2-3, 8, 16-24, and 30-32 including SEQ ID NO:10 encoding SEQ ID NO:11 are examined in the present office action.

4. Rejections and objections not set forth below are withdrawn.

5. The text of those sections of Title 35, U.S. Code not included in this office action can be found in a prior office action.

Written Description

6. Claims 2-3, 8, 16-24, and 30-32 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is maintained for the reasons of record set forth on pages 6-9 of the Official action mailed 3/14/2005, for claims 1-3, 5-6, 8, 16-24 and 30-32. Applicant's arguments filed 6/30/2005 have been fully considered but they are not persuasive.

Applicants contend that they have identified essential regions of the VRN1 protein in Example 8. Said regions comprise a putative B3 DNA binding domain, nuclear localization signals, PEST regions, RXXL motifs and a linker region (paragraph bridging pages 11 and 12 of the response of 30 June 2005).

The Office contends that Applicants have fulfilled the written description requirement for SEQ ID NO:10 encoding SEQ ID NO:11, but for nucleic acid sequences that encode a protein exhibiting less than 100% amino acid identity to SEQ ID NO:11, Applicants have not fulfilled the written description requirement. As stated in the office action mailed 3/14/2005, the written description requirement can be fulfilled by either disclosing a representative number of nucleic acid sequences encoding a VRN1 protein of SEQ ID NO:11, or a protein either from Arabidopsis or another plant, that has the same activity and function as the VRN1 protein of SEQ ID NO:11. The written description requirement can also be fulfilled by disclosing the essential regions that are required for a functional VRN1 protein of SEQ ID NO:11. One way of disclosing essential regions is to present an alignment of proteins that have the same activity and function as VRN1 of SEQ ID NO:11, wherein the proteins are from a representative number of plants. The alignment serves two functions. One, it illustrates which amino acid residues are conserved and are therefore required, and two, it illustrates the relative positions of the conserved residues one to the other.

In the instant application, Applicants have described the putative domains that are found within the VRN1 protein of SEQ ID NO:11 as compared with other proteins from Arabidopsis having different activities or functions. For example, Applicants note that the VRN1 protein of SEQ ID NO:11 has two B3 domains and then list other proteins that have a B3 domain but

composed of different residues. Applicants state, "While VRNI contains two B3 domains, most characterized and hypothetical amino acid sequences were found to contain only one B3 domain, and some were found to contain more than two. The B3 domain appears to be "defined" by a number of conserved positions (results not shown) rather than sequence identity over the whole domain. Therefore, BLAST scores between the sequences shown tested are only marginally significant (on the order of 10-6 to 10-1)" (page 47 of the specification, lines 14-21). In addition, Applicants present a phylogenetic analysis of B3 domains and conclude by stating "that through evolution the B3 domain has been recruited in different ways by proteins involved in diverse plant processes" (page 47, lines 30-32). Therefore, a B3 domain by itself does not identify a VRN1 protein of SEQ ID NO:11 or any other VRN1 protein.

In regards to the nuclear localization signals, PEST regions, RXXL motifs, Applicants state "Region 2 of VRN1 (residues 95-238), which lies between the two B3 domains (Figure 7), is not obviously related to any domain of known function, nor does it have obvious features of a transcriptional activation or repression domain. Nonetheless, region 2 does contain several sequence features and motifs of interest, including a putative nuclear localization signal, two putative PEST regions... and three RXXL motifs also associated with rapid protein degradation" (paragraph bridging pages 47-48 of the specification).

Lastly, Applicants state that the linker region is not required for the oncogenic transformation activity of the protein and that the portion of the linker region comprising the c-myc region may serve as a linker region of no great importance to VRN1 function (page 49 of the specification, lines 1-7).

Therefore, the indicated regions have not been shown to be essential for the activity and function of the VRN1 protein of SEQ ID NO:11. It still remains unclear what are the regions essential for the activity and function of Applicants' VRN1 protein of SEQ ID NO:11.

Applicants contend that the existence and sequence of a closely related Arabidopsis gene is provided in Example 8c (page 12 of the Response, 2nd paragraph).

The Office contends that the specified Arabidopsis gene, RELATED TO VRN1 (RTV1), exhibits 74% similarity to VRN1 of SEQ ID NO:11, but it has not been shown to have the same activity and function as VRN1 of SEQ ID NO:11 (See page 50 of Applicants' specification).

Applicants contend that page 12 of the specification provides a list of similar genes which share high levels of sequence similarity with VRN1 (page 12, 2nd paragraph).

The Office contends that said sequences are only EST sequences, which means that they are partial sequences and that the activity and function of the encoded protein has not been determined. Therefore, it has not been established that the disclosed sequences are in fact homologues of the VRN1 protein of SEQ ID NO:11.

Enablement

7. Claims 2-3, 8, 16-24, and 30-32 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is maintained for the reasons of record set forth on pages 9-13 of the Official action mailed 3/14/2005 for claims 1-3, 5-6, 8, 16-24 and 30-32. Applicant's arguments filed 6/30/2005 have been fully considered but they are not persuasive.

Applicants contend that they have taught how to generate a plant with altered vernalisation phenotype and they have also taught how such plants can be used. Applicants contend that they have also taught how to isolate homologous sequences encompassed by the claims (page 14 of the Response, 1st full paragraph). Applicants contend there is no undue burden of experimentation and the claimed subject matter is enabled (page 15 of the Response, top sentence).

The Office contends that Applicants have disclosed that a plant with the mutant vrn1-1 allele grown under short days exhibited an 18% reduction in leaf number after a vernalization treatment compared to a 48% reduction in leaf number of a wild-type plant. Plants with a mutant vrn1-1 allele and a mutant fca-1 allele grown under long days exhibited 14% and 27% reduction in leaf number compared with the control which exhibited a 66% reduction in leaf number (paragraph bridging pages 37-38 of specification). Applicants' claims are drawn to a plant transformed with a nucleic acid encoding a VRN1 of SEQ ID NO:11, or a method of altering the vernalization response of a plant comprising transforming a plant with a nucleic acid encoding the VRN1 protein of SEQ ID NO:11. Applicants have not disclosed how overexpressing a nucleic acid encoding a VRN1 protein of SEQ ID NO:11 will alter the vernalization response. Applicants have only given generic information pertaining to techniques that are required for transforming a plant with said nucleic acid. Therefore, given the breadth of the claims; the lack of guidance and examples; the unpredictability in the art; and the state-of-the-art, undue experimentation would be required to practice the claimed invention, and therefore the invention is not enabled.

Applicants contend that finding functional variants is readily obtainable and would not require undue experimentation (page 15 of the Response, 1st full paragraph). Applicants contend that each and every species covered by a claim need not be enabled (page 15, bottom paragraph).

The Office contends that Applicants have not disclosed a plant transformed with a nucleic acid sequence encoding a VRN1 protein of SEQ ID NO:11 in which the vernalization requirement is influenced or that the vernalization requirement is reduced. The office acknowledges that an endogenous mutant VRN1 gene of SEQ ID NO:10 affects vernalization in Arabidopsis, but Applicants' claims are drawn to an isolated nucleic acid sequence encoding a VRN1 protein of SEQ ID NO:11 or a protein exhibiting 90% identity with SEQ ID NO:11. Applicants have not disclosed a single working example in which a plant transformed with said nucleic acid exhibits the desired phenotype. Given the lack of guidance and examples; the unpredictability in the art; and the state-of-the-art as discussed in the office action mailed 3/14/2005 undue experimentation would be required to practice the claimed invention, and therefore the invention is not enabled.

Applicants contend, at page 13 of the Official Action, that no statutory basis has been provided to support the Examiner's assertion that even if Applicant were successful in arguing the issues set forth, Applicant is still limited to nucleotides 269-1295 of SEQ ID NO: 10 encoding SEQ ID NO:11.

The Office contends that the requirements for 35 U.S.C. 112 1st paragraph have not been met regarding non-exemplified fragments of SEQ ID NO:10, as stated previously.

8. Claim 22 remains rejected under 35 U.S.C. 102(b) as being anticipated by Kamada et al (1992, Plant Tissue Culture Letters 9(3):206-208). This rejection is maintained for the reasons of record set forth in the Official action mailed 3/14/2005. Applicant's arguments filed 6/30/2005 have been fully considered but they are not persuasive.

Applicants contend that Kamada et al do not disclose a VRN1 nucleotide or its encoded protein which is identical to that presently claimed, as this reference relates to a RolC encoding nucleic acid which is not SEQ ID NO:10 nor is it 90% identical to SEQ ID NO:10 (page 17 of the Response, top paragraph).

The office contends that claim 22 is drawn to a plant which is a clone or selfed or hybrid progeny or other descendant of a transgenic plant of claim 21. Due to Mendelian inheritance of genes, a single gene introduced into a parent plant would only be transferred at most to half the male gametes and half the female gametes. This translates into only three quarters of the progeny having at least a single copy of the transgene and one quarter of the progeny would not carry a copy of the transgene. Therefore, the claim reads on any hybrid progeny or other descendants from any transgenic plant, wherein said progeny or descendant do not contain a VRN1 nucleotide sequence encoding a polypeptide at least 90% identical to SEQ ID NO:11.

Applicants only state that the progeny or descendants comprise a heterologous nucleic acid wherein the heterologous nucleic acid is a VRN1 nucleotide sequence. Applicants define "VRN1" as intending to cover any of the nucleic acids that are described in the text of the specification (page 18, lines 29-30). The specification discloses that "a variant polypeptide encoded by a nucleic acid of the present invention may include within the sequence shown in Fig 7, a single amino acid or ... about 40 or 50 changes, or greater that about 50, 60, 70, 80, or 90

changes" (page 9, lines 16-20). In addition, Applicants also state "Alternatively, changes to a sequence may produce a derivative by way of one or more of addition, insertion, deletion or substitution of one or more nucleotides in the nucleic acid, leading to the addition, insertion, deletion or substitution of one or more amino acids in the encoded polypeptide" (page 9, lines 31-35).

Based on Applicants' definition of "VRN1", the Office interprets a "VRN1" nucleotide sequence to read on any nucleotide sequence because Applicants' definition reads on one base pair, or any nucleotide sequence encoding any vernalization-affecting protein.

The office contends that Kamada et al disclose a recombinant plant vector comprising the RolC gene operably linked to a promoter operable in plants and *Agrobacterium* and plant cells transformed therewith, and the regeneration of transformed plant cells into transgenic plants (page 207-208, Material and Methods section). Kamada et al disclose that *Cichorium* plants transformed with the RolC gene showed flower formation without vernalisation (page 212, top paragraph). The teachings of Kamada et al disclose a method for influencing or affecting the vernalisation phenotype of a plant comprising transforming a plant with the RolC gene. The transformed plants of Kamada et al flowered without a vernalization period, and as such, Kamada et al anticipates the claimed invention.

9. No claims are allowed.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart F. Baum whose telephone number is 571-272-0792. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on 571-272-0745. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Stuart F. Baum Ph.D.
Patent Examiner
Art Unit 1638
September 15, 2005

David T. Fox
Primary Patent Examiner
Art Unit 1638